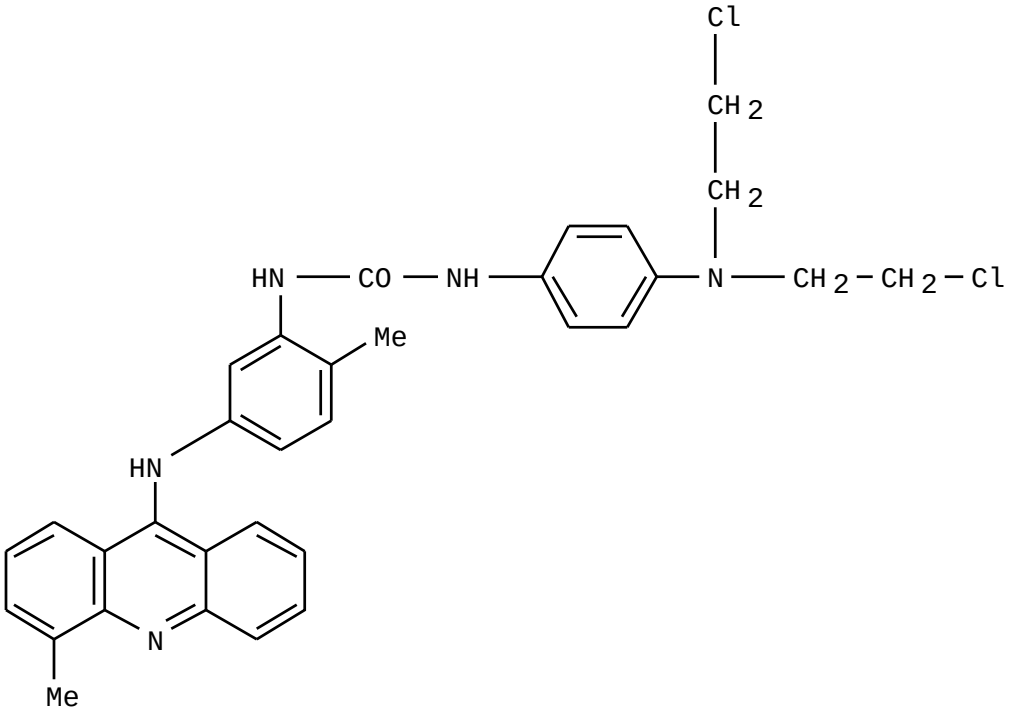
Answer 1:

Bibliographic Information

Synthesis and biological activity of stable and potent antitumor agents, aniline nitrogen mustards linked to 9-anilinoacridines via a urea linkage. Kapuriya, Naval; Kapuriya, Kalpana; Zhang, Xiuguo; Chou, Ting-Chao; Kakadiya, Rajesh; Wu, Yu-Tse; Tsai, Tung-Hu; Chen, Yu-Ting; Lee, Te-Chang; Shah, Anamik; Naliapara, Yogesh; Su, Tsann-Long. Institute of Biomedical Sciences, Laboratory of Bioorganic Chemistry, Academia Sinica, Taipei, Taiwan. Bioorganic & Medicinal Chemistry (2008), 16(10), 5413-5423. Publisher: Elsevier Ltd., CODEN: BMECEP ISSN: 0968-0896. Journal written in English. CAN 149:118685 AN 2008:642488 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

To improve the chem. stability and therapeutic efficacy of N-mustard, a series of Ph N-mustard linked to DNA-affinic 9-anilinoacridines and acridine via a urea linker were synthesized and evaluated for antitumor studies. The new N-mustard derivs. were prepd. by the reaction of 4-bis(2-chloroethyl)aminophenyl isocyanate with a variety of 9-anilinoacridines or 9-aminoacridine. The antitumor studies revealed that these agents exhibited potent cytotoxicity in vitro without cross-resistance to taxol or vinblastine and showed potent antitumor therapeutic efficacy in nude mice against human tumor xenografts. It also showed that 24d (I) was capable of inducing marked dose-dependent levels of DNA crosslinking by comet assay and has long half-life in rat plasma.



I

Answer 2:

Bibliographic Information

Predicting the active doses in humans from animal studies: a novel approach in oncology. Rocchetti, M.; Simeoni, M.;

Pesenti, E.; De Nicolao, G.; Poggesi, I. Preclinical Development, Nerviano Medical Sciences, Nerviano, Italy. European Journal of Cancer (2007), 43(12), 1862-1868. Publisher: Elsevier Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 147:461695 AN 2007:895461 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The success rate of clin. drug development is significantly lower in oncol. than in other therapeutic areas. Predicting the activity of new compds. in humans from preclin. data could substantially reduce the no. of failures. A novel approach for predicting the expected active doses in humans from the first animal studies is presented here. The method relies upon a PK/PD model of tumor growth inhibition in xenografts, which provides parameters describing the potency of the tested compds. Anticancer drugs, currently used in the clinic, were evaluated in xenograft models and their potency parameters were estd. A good correlation was obtained between these parameters and the exposures sustained at the therapeutically relevant dosing regimens. Based on the corresponding regression equation and the potency parameters estd. in the first preclin. studies, the therapeutically active concns. of new compds. can be estd. An early knowledge of level of exposure or doses to be reached in humans will improve the risk evaluation and decision making processes in anticancer drug development.

Answer 3:

Bibliographic Information

Treatment parameters modulating regression of human melanoma xenografts by an antibody-drug conjugate (CR011-vcMMAE) targeting GPNMB. Pollack, Vincent A.; Alvarez, Enrique; Tse, Kam Fai; Torgov, Michael Y.; Xie, Sam; Shenoy, Suresh G.; MacDougall, John R.; Arrol, Sharon; Zhong, Haihong; Gerwien, Robert W.; Hahne, William F.; Senter, Peter D.; Jeffers, Michael E.; Lichenstein, Henri S.; LaRochelle, William J. Department of Preclinical Development, CuraGen Corporation, Branford, CT, USA. Cancer Chemotherapy and Pharmacology (2007), 60(3), 423-435. Publisher: Springer, CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 147:377815 AN 2007:646994 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

To investigate the pharmacol. properties of the CR011-vcMMAE fully human antibody-drug conjugate (ADC), such as dose titrns., quantitation of the time (days) to complete regression, pharmacokinetics, and schedule dependency. The prior study characterized a fully human antibody to GPNMB covalently linked to monomethylauristatin E, CR011-vcMMAE, and further demonstrated cell surface staining of melanoma lines susceptible to the immunoconjugate's cytotoxicity (Clin Cancer Res 2005; 12(4): 1373-1382). The human SK-MEL-2 and SK-MEL-5 melanoma xenografts were used in athymic mice to assess anti-tumor efficacy. After s.c. implantation, tumors became established (60-100 mg), and treatment commenced by i.v. injection of the immunoconjugate or vinblastine or paclitaxel. Short-term anti-tumor effects (inhibition of tumor growth) and long-term effects (complete regression) were obsd. CR011-vcMMAE induced regression of established human SK-MEL-2 and SK-MEL-5 xenografts at doses from 1.25 to 80 mg/kg treatment when administered i.v. every 4 days (4 treatments); strikingly, regressions were not assocd. with re-growth during the observation period (200 days). The disappearance rate of implants was dose dependent (min. time, 18.5 days). Detectable serum CR011-vcMMAE $\geq$1 μg/mL (.apprx.0.01 μM) was obsd. for >30 days post-dose; CR011-vcMMAE showed an elimination half-life of 10.3 days. A low vol. of distribution suggested that CR011-vcMMAE was confined to blood and interstitial fluid. CR011-vcMMAE could be delivered by either a single bolus dose or by intermittent dosing (i.e., every 1, 2, 4, 8, or 16 days) with no discernible differences in the proportion of tumor-free survivors, indicating a lack of schedule dependency. The antibody-drug conjugate produced complete regressions, but the equiv. doses of free monomethylauristatin E or unconjugated antibody did not show anti-tumor effects. In addn., decreases in plasma tumor-derived human interleukin-8 coincided with tumor nodule disappearance.

Short-term anti-tumor effects and long-term effects (complete regression) were obsd. with CR011-vcMMAE, but not with the ref. agents. These results suggest that CR011-vcMMAE may provide therapeutic benefit in malignant melanoma.

Answer 4:

Bibliographic Information

Urease-induced alkalinization of extracellular pH and its antitumor activity in human breast and lung cancers. Wong, Wah Yau; DeLuca, Carl I.; Tian, Baomin; Wilson, Iain; Molund, Sharon; Warriar, Nalini; Govindan, Manjapra V.; Segal, Donald; Chao, Heman. Sensium Technologies Inc., Edmonton, AB, Can. Journal of Experimental Therapeutics and Oncology (2005), 5(2), 93-99. Publisher: Old City Publishing, CODEN: JETOFX ISSN: 1359-4117. Journal written in English. CAN 144:324313 AN 2005:1314419 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Jack bean urease catalyzes the decompn. of urea into ammonia, which in turn increases the pH of the surrounding medium. Based on these two properties, we have investigated the antitumor effects of urease in vitro and in vivo on human lung and breast cancer cell lines either by the enzyme itself or in combination with other chemotherapeutic drugs. First, through the generation of toxic ammonia, urease exerted direct cytotoxicity on A549 and MDA-MB-231 tumor cells with LC50 of 0.22 and 0.45 U/mL, resp. The cytotoxic effects could effectively be blocked using the reversible urease inhibitor acetohydroxamic acid. Complete protection was obsd. at dose ≥ 2 mM. In addn., nude mouse xenograft models demonstrated that intratumoral urease injections (1 - 10 U/dose) inhibited A549 and MCF-7 tumor growth in vivo. Second, when combined with weak-base anticancer drugs, urease provided indirect antitumor effects via pH augmentation. Alkalinization of extracellular pH by urease (2 U/mL) and urea (≥ 2 mM) was found to enhance the antitumor efficacy of doxorubicin (50 μM) and vinblastine (100 μM) significantly.

Answer 5:

Bibliographic Information

Effect of Mitomycin C and Vinblastine on FDG Uptake of Human Nonsmall-Cell Lung Cancer Xenografts in Nude Mice. Tian, Mei; Zhang, Hong; Higuchi, Tetsuya; Oriuchi, Noboru; Inoue, Tomio; Endo, Keigo. Dep. Nucl. med. and Diagnostic Radiol., Gunma Univ. Sch. Med., Gunma, Japan. Cancer Biotherapy & Radiopharmaceuticals (2004), 19(5), 601-605. Publisher: Mary Ann Liebert, Inc., CODEN: CBRAFJ ISSN: 1084-9785. Journal written in English. CAN 142:273277 AN 2004:991809 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study was designed to preliminarily evaluate the use of positron emission tomog. (PET) with [18F]-2-fluoro-2-deoxy-D-glucose (FDG) for monitoring chemotherapy effects, using a nude-mouse model of human nonsmall-cell lung cancer (NSCLC), the Lu-99 cell line. Tumor-FDG uptakes and vols. were measured after administrating a single dose of mitomycin (MMC) and vinblastine (VLB) and then compared these for a nontherapy group. A significant redn. in tumor vol. after either chemotherapy occurred and assocd. with significantly lower FDG uptake values than the control group ($p < 0.001$), as early as day 1. These observations suggest that FDG-PET may be useful for noninvasively monitoring the effects of cancer chemotherapy.

Answer 6:

Bibliographic Information

Fluoxetine inhibits multidrug resistance extrusion pumps and enhances responses to chemotherapy in syngeneic and in human xenograft mouse tumor models. Peer, Dan; Dekel, Yaron; Melikhov, Dina; Margalit, Rimona. Department of Biochemistry, the George S. Wise Life Science Faculty, Tel Aviv University, Tel Aviv-Jaffa, Israel. Cancer Research (2004), 64(20), 7562-7569. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 141:343083 AN 2004:858494 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Multidrug resistance (MDR) operated by extrusion pumps such as P-glycoprotein and multidrug-resistance-assocd.-proteins, is a major reason for poor responses and failures in cancer chemotherapy. MDR modulators (chemosensitizers) were found among drugs

approved for noncancer indications and their derivs. Yet toxicity, adverse effects, and poor soly. at doses required for MDR reversal prevent their clin. application. Among newly designed chemosensitizers, some still suffer from toxicity and adverse effects, whereas others progressed to clin. trials. Diversities among tumors and among MDR pumps indicate a need for several clin. approved MDR modulators. Here we report for the first time that fluoxetine (Prozac), the well-known antidepressant, is a highly effective chemosensitizer. In vitro, fluoxetine enhanced (10- to 100-fold) cytotoxicity of anticancer drugs (doxorubicin, mitomycin C, vinblastine, and paclitaxel) in drug-resistant but not in drug-sensitive cells (5 and 3 lines, resp.). Fluoxetine increased drug accumulation within MDR-cells and inhibited drug efflux from those cells. In vivo, fluoxetine enhanced doxorubicin accumulation within tumors (12-fold) with unaltered pharmacokinetics. In four resistant mouse tumor models of both syngeneic and human xenograft, combination treatment of fluoxetine and doxorubicin generated substantial ($P < 0.001$) improvements in tumor responses and in survivals (2- to 3-fold). Moreover, fluoxetine reversed MDR at doses that are well below its human safety limits, free of the severe dose-related toxicity, adverse effects, and poor soly. that are obstacles to other chemosensitizers. This low-dose range, together with the findings reported here, indicate that fluoxetine has a high potential to join the arsenal of MDR reversal agents that may reach the clinic.

Answer 7:

Bibliographic Information

Targeting vascular and avascular compartments of tumors with C. novyi-NT and anti-microtubule agents. Dang, Long H.; Bettegowda, Chetan; Agrawal, Nishant; Cheong, Ian; Huso, David; Frost, Philip; Loganzo, Frank; Greenberger, Lee; Barkoczy, Jozsef; Pettit, George R.; Smith, Amos B., III; Gurulingappa, Hallur; Khan, Saeed; Kinzler, Kenneth W.; Zhou, Shibin; Vogelstein, Bert. Howard Hughes Medical Institute and Sidney Kimmel Cancer Center, USA. Cancer Biology & Therapy (2004), 3(3), 326-337. Publisher: Landes Bioscience, CODEN: CBTAAO ISSN: 1538-4047. Journal written in English. CAN 142:106673 AN 2004:624546 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Current approaches for treating cancer are limited, in part, by the inability of drugs to affect the poorly vascularized regions of tumors. We have found that C. novyi-NT in combination with anti-microtubule agents can cause the destruction of both the vascular and avascular compartments of tumors. The two classes of microtubule inhibitors were found to exert markedly different effects. Some agents that inhibited microtubule synthesis, such as HTI-286 and vinorelbine, caused rapid, massive hemorrhagic necrosis when used in combination with C. novyi-NT. In contrast, agents that stabilized microtubules, such as the taxanes docetaxel and MAC-321, resulted in slow tumor regressions that killed most neoplastic cells. Remaining cells in the poorly perfused regions of tumors could be eradicated by C. novyi-NT. Mechanistic studies showed that the microtubule destabilizers, but not the microtubule stabilizers, radically reduced blood flow to tumors, thereby enlarging the hypoxic niche in which C. novyi-NT spores could germinate. A single i.v. injection of C. novyi-NT plus selected anti-microtubule agents was able to cause regressions of several human tumor xenografts in nude mice in the absence of excessive toxicity.

Answer 8:

Bibliographic Information

Clonogenic assay with established human tumour xenografts: correlation of in vitro to in vivo activity as a basis for anticancer drug discovery. Fiebig, H. H.; Maier, A.; Burger, A. M. Oncotest GmbH, Institute for Experimental Oncology, Freiburg, Germany. European Journal of Cancer (2004), 40(6), 802-820. Publisher: Elsevier Science Ltd., CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 141:342988 AN 2004:284718 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pluripotent cells can be grown in clonogenic assays. The tumor stem-cell fraction, which accounts for <0.4% of the total cells, and which is considered the most relevant cell type in the development of metastases and recurrences, is able to divide and to form

colonies in a semisolid matrix (agar or methylcellulose). Major applications of the tumor clonogenic assay (TCA) are chemosensitivity testing of tumors and xenografts, and for assessments within drug discovery programs. Of crit. relevance for the usefulness of the TCA is whether it can predict sensitivity or resistance towards clin. used agents. When we compared the response of human tumors established as xenografts in nude mice in the TCA in vitro to that of the clin. response, 62% of the comparisons for drug sensitivity, and 92% of the comparisons for drug resistance were correct. The same percentage of true/false observations was found when tumors were tested after serial passage in nude mice in the TCA in vitro and their response compared to in vivo activity in corresponding xenografts (60% and 90%, resp.). The highest correct predictive values were, however, found when the clin. response of tumors was compared to their explants established in the nude mouse and treated in vivo. Of 80 comparisons performed, we obsd. a correct prediction for tumor resistance in 97% and for tumor sensitivity in 90%. In our opinion, the TCA with established human tumor xenografts has an important role in current drug discovery strategies. We therefore included the TCA as secondary assay in our approach to anticancer drug discovery and found that a no. of novel agents were active; these are now in advanced preclin. development or clin. trials. Thus, the tumor clonogenic assay has proven predictive value in the chemosensitivity testing of std. and exptl. anticancer drugs.

Answer 9:

Bibliographic Information

Camptothecin analogues and vinblastine in the treatment of renal cell carcinoma: an in vivo study using a human orthotopic renal cancer xenograft. El-Galley, Rizk; Keane, Thomas E.; Sun, Carrie. Department of Urology, Emory University, Atlanta, GA, USA. Urologic Oncology: Seminars and Original Investigations (2003), 21(1), 49-57. Publisher: Elsevier, CODEN: UOSOAA Journal written in English. CAN 141:184720 AN 2004:147742 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

To perform a series of in vivo cytotoxicity studies using a variety of doses of the comptothecin analogs 9-Aminocamptothecin (9-AC) and Irinotecan (CPT-11) with a human RCC xenograft tumor line (DU11983m). Using the subrenal capsule assay (80 nude mice) (NM-SRCA), 9-AC was evaluated at both low and high dosage levels (0.75 mg/kg and 1.25 mg/kg oral ×10 doses over 12 days). Following an initial assessment of acute tumor inhibition, the study was extended to a survival assay with some cohorts receiving retreatment boluses on a once or twice weekly basis. CPT-11 was assessed at a dose of 100 mg/kg ×3 over 9 days with weekly retreatment and two cohorts received 9-AC combined with Vinblastine (2.7 mg/kg) and Vinblastine alone, resp. Tumor inhibition: tumor growth inhibition was significant (over 80%) with all cohorts receiving any camptothecin analog and was virtually complete (>99% tumor inhibition) at the high dose 9-AC (1.25 mg/kg). Vinblastine alone achieved only moderate cytotoxic effect (46%) and induced the largest recorded cohort wt. loss (toxicity). Survival anal.: the low and high dose 9-AC single agent cohorts were not significantly different; however, the CPT-11 cohort experienced maximal survival benefit. (P = 0.003) and the addn. of Vinblastine did not enhance this survival advantage among the 9-AC cohorts. Control and single agent Vinblastine cohorts had the poorest survival with the treated group still surviving longer (P = 0.02). At 35 days after final assessment of acute tumor inhibition, all animals in both the control and Vinblastine alone cohorts were dead. None of the animals in any of the other cohorts (all of which had experienced a greater than 80% tumor inhibition) had died. No deaths occurred due to surgery or treatment toxicity and all deaths were deemed tumor related. CPT-11 and 9-AC produced a marked survival advantage in an orthotopic model of human advanced renal carcinoma and are identified as agents for further clin. assessment.

Answer 10:

Bibliographic Information

Genome-wide cDNA microarray screening to correlate gene expression profiles with sensitivity of 85 human cancer xenografts to anticancer drugs. Zembutsu, Hitoshi; Ohnishi, Yasuyuki; Tsunoda, Tatsuhiko; Furukawa, Yoichi; Katagiri, Toyomasa; Ueyama, Yoshito; Tamaoki, Norikazu; Nomura, Tatsuji; Kitahara, Osamu; Yanagawa, Rempei; Hirata, Koichi; Nakamura, Yusuke. Laboratory of Molecular Medicine, Human Genome Center, Institute of Medical Science, The University of Tokyo, Tokyo, Japan. Cancer Research (2002), 62(2), 518-527. Publisher: American Association for Cancer Research, CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 136:395496 AN 2002:108259 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

One of the most crit. issues to be solved in regard to cancer chemotherapy is the need to establish a method for predicting efficacy or toxicity of anticancer drugs for individual patients. To identify genes that might be assocd. with chemosensitivity, we used a cDNA microarray representing 23,040 genes to analyze expression profiles in a panel of 85 cancer xenografts derived from nine human organs. The xenografts, implanted into nude mice, were examd. for sensitivity to nine anticancer drugs (5-fluorouracil, 3-[(4-amino-2-methyl-5-pyrimidinyl)methyl]-1-(2-chloroethyl)-1-nitrosourea hydrochloride, adriamycin, cyclophosphamide, cisplatin, mitomycin C, methotrexate, vincristine, and vinblastine). Comparison of the gene expression profiles of the tumors with sensitivities to each drug identified 1,578 genes whose expression levels correlated significantly with chemosensitivity; 333 of those genes showed significant correlation with two or more drugs, and 32 correlated with six or seven drugs. These data should contribute useful information for identifying predictive markers for drug sensitivity that may eventually provide "personalized chemotherapy" for individual patients, as well as for development of novel drugs to overcome acquired resistance of tumor cells to chem. agents.

Answer 11:

Bibliographic Information

Experimental chemotherapy against canine mammary cancer xenograft in SCID mice and prediction of its clinical effect. Yamashita, Atsuko; Maruo, Kohji; Suzuki, Kaoru; Shirota, Kinji; Kobayashi, Kimio; Hioki, Kyoji. Department of Veterinary Surgery, Tokyo University of Agriculture and Technology, Tokyo, Japan. Journal of Veterinary Medical Science (2001), 63(8), 831-836. Publisher: Japanese Society of Veterinary Science, CODEN: JVMSEQ ISSN: 0916-7250. Journal written in English. CAN 136:379575 AN 2001:706827 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effectiveness of 6 antitumor agents was evaluated for a canine mammary gland tumor (CMG-6) serially transplanted into mice with severe combined immunodeficiency. CMG-6, a solid carcinoma, was s.c. transplanted into immunodeficient mice, and 6 antitumor agents were given i.v. as a single injection. The min. EDs (MEDs; mg/kg) in mice were: cyclophosphamide (CPM) 65, doxorubicin (DXR) 6, cisplatin (CDDP) 5, vincristine (VCR) 1.6, vinblastine (VLB) >5.5, 5-fluorouracil (5-FU) 105. The clin. effects of the drugs were predicted based on the ratio of the area under the curve (AUC) in dogs given a clin. dose (AUC dog) to the AUC of mice given a MED (AUC mouse) from published refs. The AUC ratios were: CPM 2.24, DXR 0.19, CDDP 1.20, VCR 0.04, VLB <1.24 and 5-FU 1.15. The drugs having a value of >1.0 for the AUC dog/AUC mouse ratio were CPM, CDDP and 5-FU, suggesting that they might be effective in the original dogs with CMG-6. Combination chemotherapy using clin. equiv. doses of CDDP and CPM, which had the two highest values of the AUC dog/AUC mouse ratio in single-agent therapy, had addnl. effects as compared to the effectiveness of the single agents against CMG-6.

Answer 12:

Bibliographic Information

The synthesis, discovery, and development of a highly promising class of microtubule stabilization agents: curative effects of desoxyepothilones B and F against human tumor xenografts in nude mice. Chou, Ting-Chao; O'Connor, Owen A.; Tong, William P.; Guan, Yongbiao; Zhang, Zui-Guo; Stachel, Shawn J.; Lee, Chulbom; Danishefsky, Samuel J. Preclinical Pharmacology Core Facility, Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Proceedings of the National Academy of Sciences of the United States of America (2001), 98(14), 8113-8118. Publisher: National Academy of Sciences, CODEN: PNASA6 ISSN: 0027-8424. Journal written in English. CAN 135:327022 AN 2001:526491 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

We have evaluated two synthetic epothilone analogs lacking the 12,13-epoxide functionality, 12,13-desoxyepothilone B (dEpoB), and 12,13-desoxyepothilone F (dEpoF). The concns. required for 50% growth inhibition (IC50) for a variety of anticancer agents were measured in CCRF-CEM/VBL1000 cells (2,048-fold resistance to vinblastine). By using dEpoB, dEpoF, aza-EpoB, and paclitaxel, the

IC50 values were 0.029, 0.092, 2.99, and 5.17 μM, resp. These values represent 4-, 33.5-, 1,423- and 3,133-fold resistance, resp., when compared with the corresponding IC50 in the parent [nonmultiple drug-resistant (MDR)] CCRF-CEM cells. We then produced MDR human lung carcinoma A549 cells by continuous exposure of the tumor cells to sublethal concns. of dEpoB (1.8 yr), vinblastine (1.2 yr), and paclitaxel (1.8 yr). This continued exposure led to the development of 2.1-, 4,848-, and 2,553-fold resistance to each drug, resp. The therapeutic effect of dEpoB and paclitaxel was also compared in vivo in a mouse model by using various tumor xenografts. DEpoB is much more effective in reducing tumor sizes in all MDR tumors tested. Anal. of dEpoF, an analog possessing greater aq. soly. than dEpoB, showed curative effects similar to dEpoB against K562, CCRF-CEM, and MX-1 xenografts. These results indicate that dEpoB and dEpoF are efficacious antitumor agents with both a broad chemotherapeutic spectrum and wide safety margins.

Answer 13:

Bibliographic Information

Development of human lymphoma/leukemia xenograft models in immune-deficient mice for evaluation of potential anticancer agents. Dykes, D. J.; Hollingshead, M. G.; Camalier, R. F.; Waud, W. R.; Mayo, J. G. Southern Research Institute, Birmingham, AL, USA. Contributions to Oncology (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 295-304. Publisher: S. Karger AG, CODEN: COONEV ISSN: 0250-3220. Journal written in English. CAN 133:217399 AN 2000:242563 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Eleven human lymphoma/leukemia cell lines were assessed as in vivo xenograft models in severe combined immunodeficient (SCID) mice. In prepn. for efficacy evaluations of new antitumor agents, all eleven cell lines have been characterized for sensitivity to known clin. useful agents. The lines included in the study represent a variety of diseases including T-cell, myelogenous, and lymphoblastic leukemias, as well as histiocytic, B-cell and Burkitt's lymphomas. The selected agents for this study were representative of various chem. classes. Addnl., growth studies were performed including comparisons in athymic nude mice. These studies were designed to det. s.c. tumor vol. doubling times, graft success, latent growth periods, and other characteristics necessary to effectively implement and interpret anticancer efficacy evaluations. The various tumor lines used proved to be good models for chemotherapy trials. In the chemotherapy trials, considerable independent chemotherapeutic profiles were obsd. but there were also some similarities among the various histol. types.

Answer 14:

Bibliographic Information

Antitumor activity of titanocene dichloride in xenografted human renal-cell carcinoma. Kopf-Maier, P. Institut fur Anatomie, Freie Universitat Berlin, Berlin, Germany. Anticancer Research (1999), 19(1A), 493-504. Publisher: International Institute of Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 131:111022 AN 1999:298101 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Titanocene dichloride [(C5H5)2TiCl2] is a new-developed organometallic antitumor agent which is currently being investigated in clin. trials of phases I and II. In the present study, it was tested for antitumor activity in human renal tumors either growing as monolayers in vitro or as xenografts in athymic mice. For comparison, approved cytostatic drugs (in vitro, vinblastine and 5-fluoro-2'-deoxyuridine; in vivo, cyclophosphamide, vinblastine, and 5-fluorouracil) were administered in vitro and in vivo at equiv. or equitoxic dose levels, resp. Under in vitro conditions, titanocene dichloride was active only moderately. When it was applied at peak plasma level of 104 mol/l, it induced cell growth inhibitions by 25-50% in all KTCTL cell lines investigated (KTCTL-1M, KTCTL-2, KTCTL-26A, KTCTL-30, KTCTL-84). In the N-U 2 carcinoma cell strain it was more effective and caused cell growth inhibitions of 70-80% at the 10-4 mol/l level, the IC50 value amounting to 5 × 10-6 mol/l. When titanocene dichloride was applied i.p. according to the Q3Dx5 and Q2Dx5 regimens and investigated in the human renal-cell carcinoma N-U 2 growing as xenograft in athymic mice, it

brought about significant and dose-dependent growth redns. by 50-75% in relation to untreated controls, whereas cyclophosphamide given as single bolus injection and vinblastine administered both as single and triple doses were slightly less effective in this xenograft. MKT 4 and MKT 5, two formulations of titanocene dichloride which are currently used in clin. trials, showed similar efficacy as titanocene dichloride towards the N-U 2 renal-cell carcinoma xenograft. In the heterotransplanted N-U 26 carcinoma, titanocene dichloride induced relative growth redns. by 50-56% and was similarly active as cyclophosphamide, but less effective than vinblastine applied as a single dose. Titanocene dichloride was again significantly active in the KTCTL-1M carcinoma xenograft and caused relative growth redns. by 50-65%.

In the case of the MRI-H 121 renal sarcoma xenograft, however, the organometallic compd. showed an only marginal activity which was surpassed by cyclophosphamide, vinblastine and 5-fluorouracil, all three drugs inducing significant relative growth inhibitions by 50-88%. These results confirm a significant and remarkable antitumor activity of titanocene dichloride in three out of four human renal tumors xenografted to athymic mice and suggest that clin. studies of phase ll with titanocene dichloride towards renal-cell carcinoma in human patients should be done in the near future.

Answer 15:

Bibliographic Information

The alkylator treosulfan shows activity towards human renal-cell carcinoma in vivo and in vitro. Koepf-Maier, P. Institut fuer Anatomie, Freie Universitaet Berlin, Berlin, Germany. In Vivo (1998), 12(3), 275-288. Publisher: International Institute of Anticancer Research, CODEN: IVIVE4 ISSN: 0258-851X. Journal written in English. CAN 129:285676 AN 1998:550055 CAPLUS

Abstract

Treosulfan (L-threitol-1,4-bismethanesulfonate, Ovastat) was tested on human renal tumor cells growing as xenografts in athymic nude mice and as monolayers in vitro, in comparison with clin. used cytostatic drugs (in vivo, cyclophosphamide, vinblastine, and 5-fluorouracil; in vitro, vinblastine and 5-fluoro-2'-deoxyuridine) which were administered at equitoxic or equiv. dose levels, resp. Four human renal tumor xenografts (N-U 2, N-U 26, MRI-H 121, KTCTL-1M) were investigated in vivo, and seven renal tumor cell lines (KTCTL-1M, KTCTL-2, KTCTL-26A, KTCTL-30, KTCTL-84, MRI-H 121, N-U 2) under in vitro conditions. The investigations of the four human renal tumor xenografts revealed that treosulfan is capable of inducing pronounced growth inhibitions ranging from 60-100% in comparison with untreated control tumors. In the xenografted renal-cell carcinoma KTCTL-1M, treosulfan administered at the highest dose level (1 × 3500 mg/kg) even effected a complete remission lasting for more than three weeks in all animals treated with this dose. It was more effective in the N-U 2 carcinoma growing in vivo than the comparative compds. cyclophosphamide and vinblastine. In the heterotransplanted renal-cell carcinoma N-U 26, treosulfan showed a similar activity as the two established cytostatic drugs tested whereas, in the renal sarcoma MRI-H 121, both cyclophosphamide and vinblastine were slightly more effective than treosulfan. In four renal-cell carcinomas growing as monolayers in vitro (KTCTL-1M, KTCTL-2, KTCTL-84, N-U 2), treosulfan induced cell growth inhibitions by about 50% at peak plasma concn. in comparison with untreated control cultures. The IC50 values ranged from 5 × 10-6 to 10-4 mol/L in all seven monolayer cultures investigated. 5-Fluoro-2'-deoxyuridine (floxuridine) was similarly active in vitro as treosulfan with respect to the molar concns.

inducing growth inhibition and to the IC50 values, whereas vinblastine was more effective than treosulfan in most of the human renal tumor cell monolayers investigated. These results reveal the remarkable antitumor efficacy of treosulfan toward human renal-cell carcinomas, esp. under in vivo conditions. This activity was similarly high or even better than in cyclophosphamide and vinblastine. The in vitro data obtained in monolayer cultures also confirmed the remarkable antiproliferative activity of treosulfan in renal tumor cells, but did not mirror very well the pattern of antitumor activity obsd. in vivo.

Answer 16:

Bibliographic Information

Antitumor effect of CPT-11, a camptothecin derivative, on human testicular tumor xenografts in nude mice. Miki, Tsuneharu; Sawada, Masumi; Nonomura, Norio; Kojima, Yasuyuki; Okuyama, Akihiko; Maeda, Osamu; Saiki, Shigeru; Kotake, Toshihiko. Department of Urology, Osaka University Medical School, Osaka, Japan. European Urology (1997), 31(1), 92-96. Publisher: S.

Karger AG, CODEN: EUURAV ISSN: 0302-2838. Journal written in English. CAN 129:285665 AN 1998:542001 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor effect of CPT-11, a camptothecin deriv., on two human testicular embryonal carcinomas (TTSC-2 and TTSC-3) heterotransplanted into nude mice was studied. Tumor-bearing nude mice were given daily i.p. injections of the anticancer drugs in 0.1 mL saline 3 times at 3-day intervals. At the end of the expts. tumors were resected and subjected to light-microscopic observation. When 10, 30 and 50 mg/kg of CPT-11 was administered to tumor-bearing mice i.p., the antitumor effect of CPT-11 was obsd. dose-dependently in both TTSC-2 and TTSC-3. When 30 mg/kg of CPT-11 was administered in combination with CDDP, complete tumor regression was obsd. in both TTSC-2 and TTSC-3 tumors. Histol. findings correlated well with the decrease in tumor vol. of treated tumors. No mice died after treatment with CPT-11 in a single-agent and combination chemotherapy. Chemotherapy with CPT-11 was an effective and safe method against human testicular tumors heterotransplanted in nude mice.

Answer 17:

Bibliographic Information

The efficacy of 2',2'-difluorodeoxycytidine (gemcitabine) and vinblastine combined with interferon in nude mice xenografts of human renal cell carcinoma. Rohde, Detlef; Goertz, Markus; Blatter, Johannes; Jakse, Gerhard. Department of Urology, Medical Faculty, University of Aachen, Aachen, Germany. International Journal of Oncology (1998), 12(6), 1367-1372. Publisher: International Journal of Oncology, CODEN: IJONES ISSN: 1019-6439. Journal written in English. CAN 129:144586 AN 1998:366966 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Recent in vitro expts. indicated strong activity of 2',2'-difluorodeoxycytidine (dFdC, gemcitabine) in human renal cell carcinoma (RCC) cell lines and an increase of efficacy by combined application of interferon (IFN). In the present study, nude mice with xenografts from ACHN- or SN12C cells were treated by dFdC, dFdC plus IFN-α or vinblastine (VBL) plus IFN-α. ACHN-xenografts were significantly more inhibited by dFdC+/-IFN-α than by VBL+IFN-α. Complete remissions (CR) were only seen by dFdC. An addnl. treatment with IFN-α shortened the time to commencement of tumor remission and increased CR of ACHN- and SN12C-tumors (40%; 7%) compared to a treatment with dFdC alone (20%; 0). DFdC+IFN-α reduced the no. of pulmonary metastases compared to untreated animals. Survival was significantly prolonged by dFdC+/-IFN-α in ACHN-mice and dFdC+IFN-α or VBL+IFN-α in SN12C mice. In conclusion, exptl. data confirm dFdC as a superior drug against human RCC compared to VBL. Combined therapy with IFN-α increased the efficacy of dFdC in terms of tumor response in immunodeficient nude mice, thus clin. studies are strongly recommended in patients with metastatic renal cell carcinoma.

Answer 18:

Bibliographic Information

Establishment and serial quantification of intrahepatic xenografts of human hepatocellular carcinoma in severe combined immunodeficiency mice, and development of therapeutic strategies to overcome multidrug resistance. Leveille-Webster, Cynthia R.; Arias, Irwin A. School Medicine, Tufts University, Boston, MA, USA. Clinical Cancer Research (1996), 2(4), 695-706. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 124:332166 AN 1996:261680 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A murine model in which to study multiple drug resistance in human hepatocellular carcinoma was developed. PRF/PLC/5 hepatoma cells (Alex 0) and an induced multidrug resistant clone (Alex 0.5) were injected intrasplenically into severe combined immunodeficiency mice. In 70% of injected mice, hepatoma cells engrafted in the liver and grew as intrahepatic metastasis. Since Alex cells contain an

integrated hepatitis B virus genome and secrete hepatitis B surface antigen (HBsAg), the serum HBsAg concn. in tumor-bearing mice was used to quantitate tumor burden. Tumor wet wt. detd. at necropsy was directly proportional to the serum HBsAg concn. In Alex 0 cells, IC50s for doxorubicin, vinblastine, and cis-platinum were 0.35 μM, 0.029 μM, and 3.70 μM, resp. Alex 0.5 cells were 25-, 14-, and 1.4-fold more resistant to doxorubicin, vinblastine, and cis-platinum, resp. Immunoblotting of Alex 0 cell membranes with an anti-P-glycoprotein antibody (C219) revealed small amts. of P-glycoprotein, whereas Alex 0.5 membranes overexpressed the protein. Concurrent exposure to verapamil (10 μM) sensitized both cell lines to the cytotoxic action of vinblastine and doxorubicin but had no effect on the cytotoxicity of cis-platinum. Mice bearing intrahepatic xenografts derived from Alex 0 and 0.5 cells had no response to treatment with i.v. vinblastine or doxorubicin, as was anticipated from in vitro drug testing. Addn. of verapamil to vinblastine treatment did not improve the success of in vivo chemotherapy. Immunotherapy with a human anti-P-glycoprotein antibody (MRK16) suppressed the in vivo growth of tumors derived from both cell lines. The effect was most pronounced in mice bearing Alex 0.5 tumors. Immunoblotting of tumors which initially responded to MRK16 therapy, but subsequently relapsed, revealed a marked decrease in P-glycoprotein expression when compared to results in tumors that were untreated or treated with vinblastine or control antibody.
In summary, we have developed an intrahepatic tumor xenograft model of human hepatocellular carcinoma in mice that permits noninvasive serial quantification of tumor burden by detn. of serum HBsAg levels and demonstrated a pos. response to immunotherapy with anti-P-glycoprotein antibodies.

Answer 19:

Bibliographic Information

Comparative antitumor activity of vinblastine-isoleucinate and related vinca alkaloids in human tumor xenografts. Hendriks, Hans R.; Langdon, Simon; Berger, Dietmar P.; Breistoel, Knut; Fiebig, Heinz H.; Fodstad, Oeystein; Schwartsmann, Gilberto. EORTC New Drug Dev. Off., Free Univ. Hosp., Amsterdam, Neth. Eur. J. Cancer, Part A (1992), 28A(4-5), 767-73. CODEN: EJCTEA Journal written in English. CAN 117:184418 AN 1992:584418 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of the investigational agent vinblastine-isoleucinate (V-LEU) was compared with vintriptol, another investigational agent of the same series of vinblastine-23-oyl amino acid derivs., and vinblastine, their clin. active parent compd., in a panel of nine human tumor xenografts growing s.c. in nude mice. Compds. were administered i.v. at equitoxic doses twice weekly. As assessed by optimal tumor growth inhibition and tumor growth delay, vinblastine, V-LEU and vintriptol exhibited antitumor activity in 8/9, 7/9 and 4/7 human tumor xenografts, resp. When growth curves and nos. of complete remissions were compared, V-LEU was the most active agent in two malignant melanoma lines (THXO and LOX p28) and two small cell lung carcinoma lines tested (LXFS 528 and WX 322), whereas vinblastine was more active against the two colorectal carcinomas (CXF 243 and CXF 280). Notably, the non-small cell lung carcinoma (NSCLC) line AHXOL was resistant to the three agents. The results of this study suggest that V-LEU was as active as vinblastine in most tumor lines, exhibiting superior antitumor activity in malignant melanoma, SCLC and breast cancer lines.

Answer 20:

Bibliographic Information

Suppression of well-established tumor xenografts by a hybrid-hybrid monoclonal antibody and vinblastine. Smith, W.; Gore, V. A.; Brandon, D. R.; Lynch, D. N.; Cranstone, S. A.; Corvalan, J. R. F. Lilly Res. Cent. Ltd., Eli Lilly and Co., Windlesham/Surrey, UK. Cancer Immunology Immunotherapy (1990), 31(3), 157-63. CODEN: CIIMDN ISSN: 0340-7004. Journal written in English. CAN 113:178118 AN 1990:578118 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The hybrid-hybrid monoclonal antibody 28-19-8 has specificity for the tumor-assocd. antigen carcinoembryonic antigen and the vinca alkaloids. This bifunctional antibody was used to target unmodified vinblastine sulfate to well-established MAW1 human tumor xenografts implanted in nude mice. The highly significant suppression of tumor growth achieved throughout treatment was also

sustained for over 2 mo after the withdrawal of treatment. Histol. examn. of excised tumors from treated animals has shown profound changes in their morphol. when compared with tumors from control animals. Cells in tumors that had started to grow again after withdrawal of therapy were shown still to express carcinoembryonic antigen, the target antigen recognized by the bispecific antibody.

Answer 21:

Bibliographic Information

Increased therapeutic effect of Vinca alkaloids targeted to tumor by a hybrid-hybrid monoclonal antibody. Corvalan, J. R. F.; Smith, W.; Gore, V. A.; Brandon, D. R.; Ryde, P. J. Lilly Res. Cent. Ltd., Eli Lilly and Co., Surrey, UK. Cancer Immunology Immunotherapy (1987), 24(2), 138-43. CODEN: CIIMDN ISSN: 0340-7004. Journal written in English. CAN 107:70352 AN 1987:470352 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Unmodified vinblastine (VLB) targeted through one of the antigen combining sites of the hybrid-hybrid 29.19.8 monoclonal is potentially more effective in suppressing the growth of established MAWI tumor xenografts implanted on nude mice than free VLB in the absence of the targeting agent, presumably due to an increased local drug concn. Results in this study suggest that drug, specifically removed from the circulation by hybrid-hybrid antibody previously located to the tumor mass, can be made available in a pharmacol. active from. Histol. anal. of the treated tumors revealed dramatic changes in the tumor organization with only a few surviving tumor cells with altered morphol.

Answer 22:

Bibliographic Information

Xenografts in pharmacologically immunosuppressed mice as a model to test the chemotherapeutic sensitivity of human tumors. Floersheim, G. L.; Bieri, A.; Chiodetti, Nicole. Zent. Lehre Forsch., Kantonssp., Basel, Switz. International Journal of Cancer (1986), 37(1), 109-14. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 104:81665 AN 1986:81665 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A human tumor xenograft model using pharmacol. immunosuppressed mice was assessed for its suitability to test preclinically the sensitivity of colorectal carcinomas, bone sarcomas and melanomas against anticancer agents. Beside ionizing radiation, 14 cytotoxic drugs including 5-fluorouracil (5-FU) [51-21-8], dimethylmyleran (DMM) [55-93-6], cytosine arabinoside [147-94-4], cyclophosphamide [50-18-0], melphalan [148-82-3], mitomycin C [50-07-7], adriamycin [23214-92-8], bleomycin [11056-06-7], etoposide [33419-42-0], vinblastine [865-21-4], cisplatin [15663-27-1], procarbazine [671-16-9], DTIC [4342-03-4], and BCNU [154-93-8] were assayed. Ionizing radiation, 5-FU and DMM were also applied at LDs followed by bone-marrow rescue high-dose therapy. Four colon carcinomas responded poorly to most of the agents but one tumor displayed marked sensitivity to BCNU. LDs of radiation, 5-FU and DMM and cyclophosphamide and by an osteosarcoma to the latter drug. No strong effects were seen against melanomas. LDs of DMM induced the best regression of one colon carcinoma. In general, the superiority of high-dose therapy for solid human tumors compared to maximally tolerated doses was demonstrated. Individual carcinomas of the same type displayed different drug sensitivity.

Answer 23:

Bibliographic Information

Screening test of antitumor agents by human tumor cell lines in nude mice in ascitic form. Kitahara, Takeshi; Minato, Keisuke; Shimoyama, Masanori. Natl. Cancer Cent. Hosp., Japan. Gan no Rinsho (1984), 30(9), 1158-67. CODEN: GANRAE ISSN: 0021-4949. Journal written in Japanese. CAN 102:17008 AN 1985:17008 CAPLUS (Copyright (C) 2008 ACS on

SciFinder (R))

Abstract

Human breast cancer and leukemic cells implanted in nude mice appeared to be useful models for the screening of neoplasm inhibitors. The sensitivities of implanted tissues to drugs were similar to those found in patients. Studies on the suitable route of administration in these mice provide the best administration routes for humans.

Answer 24:

Bibliographic Information

Drug testing using a soft agar stem cell assay on patient and xenograft tumor material. Hanson, Jane; Coombs, Annie; Moore, John L. Radiobiol. Dep., Velindre Hosp., Whitchurch/Cardiff, UK. International Journal of Radiation Oncology, Biology, Physics (1984), 10(9), 1697-701. CODEN: IOBPD3 ISSN: 0360-3016. Journal written in English. CAN 102:17003 AN 1985:17003 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Fifty tumor samples from 10 different sites were studied. Over half were breast or ovarian tumors. Of the 27 that were considered suitable for cloning, 11 produced colony formation and 6 of these were drug tested. One ovarian granulosa cell tumor and its mouse xenograft (V7) were tested against several cytotoxic agents. During a period of 16 mo, sensitivity to cisplatin [15663-27-1] was relatively stable but sensitivity to vinblastine [865-21-4] was markedly changed when the original tumor cells and original cells stored in liq. N were compared with xenograft cells. These changes may be related to patient treatments prior to tumor sample collection. Gross histol. of original tumor and xenograft were similar. Chemosensitization in vivo of a breast xenograft (Hx99) to melphalan [148-82-3] by misonidazole [13551-87-6] was investigated. Misonidazole at a total dose of 0.5 g/kg given prior to melphalan (14 mg/kg) was an effective chemosensitizer.

Answer 25:

Bibliographic Information

Determinants of intrinsic sensitivity to Vinca alkaloids in xenografts of pediatric rhabdomyosarcomas. Houghton, Janet A.; Williams, Larry G.; Torrance, Pamela M.; Houghton, Peter J. Dep. Biochem. Clin. Pharmacol., St. Jude Children's Res. Hosp., Memphis, TN, USA. Cancer Research (1984), 44(2), 582-90. CODEN: CNREA8 ISSN: 0008-5472. Journal written in English. CAN 100:96286 AN 1984:96286 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Three pediatric rhabdomyosarcoma xenografts maintained s.c. in immune-deprived mice differed in their sensitivity to vincristine (VCR) [57-22-7] and vinblastine (VBL) [865-21-4]; 2 lines (Rh12 and Rh28) were extremely sensitive to VCR, whereas Rh18 tumors were less sensitive. Rh28 tumors were also very responsive to VLB, which demonstrated only marginal activity in the other 2 lines. After administration of equimolar doses (3 mg/kg) of [3H]VCR and [3H]VLB to tumor-bearing mice, [3H]VCR reached concns. approaching 1.5 μM in cell water of each tumor line within 4 h, at which time >93% of the drug was cell-assocd. The drug was subsequently retained at this level for at least 72 h. [3H]VLB accumulated to lower maximal concns. (approx. 1 μM) within 8 h, but was not retained and, by 72 h, reached concns. that were 3- to 4-fold lower than those of [3H]VCR. The extent of drug retention correlated with the antitumor activity, except in Rh28 tumors, which were sensitive to VLB, but did not retain the drug. The threshold level for achieving cytotoxicity may, thus, be very low in this line. In normal tissues, maximal concns. of both [3H]VCR and [3H]VLB were achieved within 1 h of administration i.p. to tumor-bearing mice. In ileum, liver, and kidney, these were approx. 10-fold higher than the peak levels achieved within tumors or plasma, but declined rapidly to parallel the decrease in plasma, reaching concns. >5-fold lower than the concn. of [3H]VCR in tumors at 72 h after treatment. Drug concns. in skeletal muscle also declined rapidly, whereas neither

[3H]VCR nor [3H]VLB accumulated to any great extent in brain. The blood vols. of ileum, kidney, and liver were greater than for tumor tissues. Hence, the extent of drug delivery did not necessarily influence therapeutic selectivity. In the case of [3H]VLB, concns. in tumors approached those of normal tissues at 72 h after injection.
By 24 h after treatment, 86-99% of [3H]VCR and 78-90% of [3H]VLB were present in tumors as the parent compd., which also predominated in normal tissues. Metabolites or in vivo degrdn. products were also identified. Hence, selective retention in tumors appears to be the mechanism by which therapeutic selectivity is achieved with VCR in rhabdomyosarcoma xenografts. The general lack of metab. by normal tissues suggests that metab. may not influence retention in these tissues. The importance of the interaction of these agents with tubulin in different tissues as well as factors influencing drug retention are discussed.

Answer 26:

Bibliographic Information

Chemotherapy of human yolk sac tumor heterotransplanted in nude mice. Sawada, Masumi; Matsui, Yoshiaki; Okudaira, Yoshio. Res. Inst. Microb. Dis., Osaka Univ., Suita, Japan. JNCI, Journal of the National Cancer Institute (1983), 71(6), 1221-5. CODEN: JJIND8 ISSN: 0198-0157. Journal written in English. CAN 100:96258 AN 1984:96258 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The chemotherapeutic effects of cis-diamminedichloroplatinum [15663-27-1] plus vinblastine [865-21-4] plus bleomycin [11056-06-7] (PVB) on 3 human yolk sac tumors (YST-1, YST-2, and YST-3) of the ovary, which were heterotransplanted into BALB/c nude mice, were compared with the effects of vincristine+actinomycin D+cyclophosphamide (VAC), the combination currently favored for treatment of yolk sac tumors. Both PVB and VAC significantly reduced the tumor vol. of all the treated tumors. The mean wts. of tumors in animals treated with PVB or VAC were, in percent of the mean tumor wt. in untreated animals: 1.3 and 1.6 for YST-1, 2.5 and 3.3 for YST-2, and 5.5 and 2.7 for YST-3, resp. A strong correlation was noted between tumor vol. and α-fetoprotein level in the sera of mice bearing YST-1 or TST-2 tumors.

Answer 27:

Bibliographic Information

Chromatographic analysis of vinca alkaloids in human neoplastic tissues and host (mouse) tissues after injection in vivo or after incubation in vitro. Houghton, Janet A.; Torrance, Pamela M.; Houghton, Peter J. Dep. Biochem. Clin. Pharmacol., St. Jude Child. Res. Hosp., Memphis, TN, USA. Analytical Biochemistry (1983), 134(2), 450-4. CODEN: ANBCA2 ISSN: 0003-2697. Journal written in English. CAN 99:205460 AN 1983:605460 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

A method for extg. vinblastine [865-21-4], vincristine [57-22-7], and their metabolites from biol. samples, with subsequent anal. by high-performance liq. chromatog., has been developed. After excision, tissues are rapidly frozen in liq. nitrogen (<10 s) and powders are made under liq. N2. Extn. of blood, plasma, or tissue powders was achieved using EtOH (95%) acidified to pH 4.9 with acetic acid. Exts. were analyzed using reverse-phase chromatog. capable of sepg. Vinca alkaloids with substitutions on the vindoline or catharanthine moiety. This technique was used to elucidate the metab. of vincristine and vinblastine in a human rhabdomyosarcoma growing as a xenograft in immune-deprived mice and in host tissue and fluid.

Answer 28:

Bibliographic Information

In vitro sensitivity of human melanoma xenografts to cytotoxic drugs. Correlation with in vivo chemosensitivity. Tveit, Kjell Magne; Fodstad, Oeystein; Olsnes, Sjur; Pihl, Alexander. Norwegian Cancer Society, Norsk Hydro's Inst. Cancer Res., Oslo, Norway. International Journal of Cancer (1980), 26(6), 717-22. CODEN: IJCNAW ISSN: 0020-7136. Journal written in English. CAN 94:76807 AN 1981:76807 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Single-cell suspensions prepd. from 5 human melanomas, grown serially as xenografts in athymic nude mice, were exposed in vitro to increasing concns. of dacarbazine [4342-03-4], CCNU [13010-47-4], procarbazine [671-16-9], vinblastine [865-21-4], and the cancerostatic lectins abrin and ricin. The in vitro chemosensitivity of the cells, as measured by the drug concns. required to inhibit colony formation in soft agar by 50%, was correlated with the growth delay of the xenografts in vivo, previously obsd. after treatment of the animals with maximal tolerable doses of the same drugs. For each drug, the in vitro sensitivity of the different xenografts was strongly correlated with their response in vivo. Apparently, the soft agar test, as carried out here, adequately reflects the relative sensitivity of the xenografts in vivo. The data indicate that human xenografts may be used to develop quant. in vitro chemosensitivity tests.

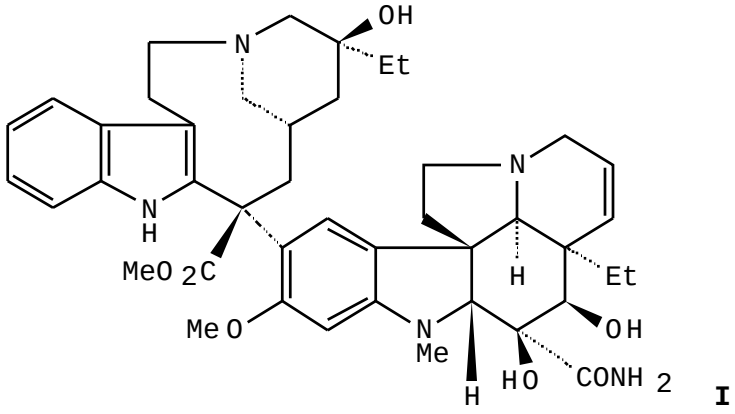
Answer 29:

Bibliographic Information

Effect of desacetyl vinblastine amide (DVA) against human sarcomas heterotransplanted in nude mice. Sordillo, Peter P.; Hajdu, Steven I.; Magill, Gordon B.; Lesser, Martin; Helson, Lawrence. Mem. Sloan-Kettering Cancer Cent., New York, NY, USA. Cancer Clinical Trials (1980), 3(4), 391-4. CODEN: CCTRDH ISSN: 0190-1206. Journal written in English. CAN 93:230906 AN 1980:630906 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The efficacy of desacetyl vinblastine amide (I) [53643-48-4] was tested against 5 human sarcomas heterotransplanted into nude mice. Marked antitumor effect was found against a lipoblastic liposarcoma, including complete regressions of tumor in some animals. A lesser, though statistically significant, antitumor effect was obsd. with a malignant schwannoma. No antitumor activity was seen against a leiomyosarcoma, epithelioid sarcoma, or Erwing's sarcoma. Thus, I deserves study in the treatment of human patients with malignant sarcomas.



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Answer 30:

Bibliographic Information

In vivo antitumor activity demonstrated with squamous carcinoma reactive monoclonal antibody-Vinca immunoconjugates. Johnson D A; Zimmermann J L; Laguzza B C; Eble J N Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, In 46285 Cancer immunology, immunotherapy : CII (1988), 27(3), 241-5. Journal code: 8605732. ISSN:0340-7004. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 3180148 AN 89028529 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

An immunoconjugate (PF1/D-DAVLBHYD), made with the squamous carcinoma reactive monoclonal antibody PF1/D and a derivative of vinblastine, DAVLBHYD, was shown to suppress established T222 human tumor nude mouse xenografts using a multidose protocol. Treatments of xenograft-bearing mice with free drug, free antibody, or a mixture of the two, were unsuccessful at achieving suppression without associated toxicity, using otherwise identical protocols. A Vinca conjugate with a related squamous carcinoma reactive monoclonal antibody, PF1/B, was shown to have similar tumor suppressive activity. In a dual immunoconjugate therapy protocol, PF1/D-DAVLBHYD and PF1/B-DAVLBHYD had additive antitumor effects which were consistent with their complementary tumor reactivity.